REMARKS

Claims 1-23 are pending. Claims 1-12 are withdrawn. Claims 13-23 are under consideration. Claims 13-23 are rejected. Claims 16 and 21-23 are objected to. Claims 13, 15-19, and 21-23 are amended. Claims 24 and 25 are new. Reconsideration and allowance of the pending claims in light of the foregoing amendments and the following remarks are respectfully requested.

Acknowledgement of Rejoinder of Groups II and III

In an Office Action dated November 17, 2008, the Examiner restricted the claims to three groups: Groups I (claims 1-12), II (claims 13-15) and III (claims 16-23). Applicants traversed the rejection in their Response filed December 17, 2008. Consequently, the Examiner rejoined Groups II and Groups III.

Claim Objections

The Examiner objected to the use of the acronym "TNFα" in claims 16, and 21-23. Accordingly, Applicants have spelled out the acronym in those claims. Applicants respectfully request withdrawal of the objection.

Claim Rejections Under 35 USC 112, Second Paragraph

The Examiner rejected claims 13-23 under 35 USC 112, second paragraph, for being indefinite for containing the term "and/or", contending that this term does not constitute proper Markush group language. Accordingly, Applicants have amended claims 13, 17, and 19 to omit this term and to provide a proper Markush group. Applications respectfully request reconsideration and withdrawal of the rejection under 35 USC 112, second paragraph.

Claim Rejections Under 35 USC 102(b)

The Examiner rejected claims 13 and 14 under 35 USC 102(b), contending they are anticipated by Okada et al. (EP 1174148).

Contrary to the Examiner's assertions, Okada et al. fails to teach the claimed invention of claims 13 and 14 because the compositions described in Okada et al. are specific to humanized monoclonal antibody ***fragments***, specifically Fab fragments. Furthermore, Okada et al. teaches that the preferred antibody fragment concentration is ***0.01 to 10 mg/ml***, and more preferably ***0.1 to 8 mg/ml*** (see page 3, line 10).

In contrast, Applicants' claims 13 and 14 are directed to aqueous pharmaceutical compositions comprising an antibody, *i.e.*, a ***complete antibody***. Okada et al. fails to teach or suggest a composition comprising a complete antibody. In addition, amended claims 13 and 14 require that the pharmaceutical compositions comprise an antibody at a ***concentration of between about 20 and 130 mg/ml***. Thus, the teachings of Okada et al. fail to teach Applicants' invention of an aqueous pharmaceutical composition comprising an ***antibody*** at high antibody concentration, i.e., an ***antibody concentration of between about 20 and 130 mg/ml***.

In view of the foregoing, Applicants respectfully submit that Okada et al. does not anticipate claims 13 and 14 and respectfully request reconsideration and withdrawal of the rejection under 35 USC 102(b).

Claim Rejections Under 35 USC 102(e)

The Examiner rejected claims 13 and 14 under 35 USC 102(e), contending they are anticipated by Gombotz et al. (US 20030180287).

Applicants submit that Gombotz et al. does not identically disclose the claimed invention of claims 13 and 14. Gombotz et al. discloses and claims ***Fc domain containing polypeptide formulations that contain either L-arginine or L-cysteine***. Gombotz et al. discloses that, optionally, the composition can include a buffer, a tonicity modifier and one or more excipients. Applicants further submit that the Fc domain containing polypeptides disclosed in Gombotz et al. are ***Fc domain fusion proteins***, such as a soluble form of the TNF receptor fused to an Fc domain. Gombotz et al. mentions the use of antibodies in his L-arginine- or L-cysteine-containing formulations but provides no guidance data on the suitability of such formulations.

Applicants submit that claims 13-25 do not recite compositions or formulations containing ***either L-arginine or L-cysteine***, nor do claims 13-25 recite ***Fc domain fusion proteins***. Applicants submit that claims 13-25 recite either whole antibodies or antigen binding portions thereof.

In view of the foregoing, Applicants respectfully submit that Gombotz et al. does not anticipate claims 13 and 14 and request reconsideration and withdrawal of the rejection under 35 USC 102(e).

Claim Rejections Under 35 USC 103(a)

The Examiner rejected claims 15, 17, 18, and 19 under 35 USC 103(a), contending they are unpatentable over Okada et al. (EP 1174148) and Gombotz et al. (US 20030180287).

Okada et al. and Gombotz et al. are discussed above. Applicants submit that there is no motivation to combine these two references, which are directed at formulating either low concentration Fab fragments (Okada et al.) or Fc domain containing polypeptides, namely Fc domain fusion proteins, or antibodies, formulated in ***either L-arginine and L-cysteine***. Even if the references were combinable, their disclosures would not teach Applicants claimed invention, which does not contain L-arginine and L-cysteine.

Applicants respectfully disagree with the Examiner's contention that a person of ordinary skill in the art would have a reasonable expectation of success and that such formulations are routine. Okada et al. and Gombotz et al. fail to teach or suggest the specific amounts and combination of ingredients required by the claimed formulations of claims 13-25, either alone or in combination, which formulations Applicants have demonstrated through a working example in the instant Specification results in a pharmaceutical formulation with both **improved shelf life and the ability to dissolve high concentrations of proteins** (see examples 1 and 2 at pages 28-30 of instant Specification). Applicants submit that it would **not** have been obvious to one of ordinary skill in the art, based on the teachings of US 6,060,382 and Gombotz et al., to combine the specific ingredients of the claims to arrive at a pharmaceutical formulation with **improved stability and/or a high protein concentration**.

As indicated above, the claimed formulations are inventive in that they embody Applicants' **unexpected discovery** that the claimed formulations are effective in **improving the stability of an antibody at high antibody concentration in the liquid state**. US 6,060,382 fails to teach or suggest pharmaceutical compositions or formulations comprising **a liquid aqueous formulation comprising an antibody with improved stability and/or a high protein concentration**. Thus, US 6,060,382 would not render the claimed invention obvious to the ordinarily skilled artisan.

Claim Rejections Under 35 USC 103(a)

The Examiner rejected claim 16 and 21-23 under 35 USC 103(a), contending they are unpatentable over Gombotz et al. (US 20030180287) in view of Salfeld et al. (US 6,060,382).

Gombotz et al. is discussed above.

US 6,060,382 does not cure the deficiencies of Gombotz et al. as a reference such that their combination renders Applicants' claimed invention obvious.

US 6,060,382 teaches fully human anti-TNFα antibodies. US 6,060,382 further teaches that pharmaceutical formulations comprising such antibodies may be prepared, for example, by using PBS, isotonic agents, emulsifying agents or surfactants. US 6,060,382 fails to teach or suggest a composition or formulation comprising an antibody at a concentration between about 20 and about 130 mg/ml, as required by claims 13 and 14, or between about 2 and about 150 mg/ml, as required by claims 17-25. US 6,060,382 also fails to teach or suggest an aqueous pharmaceutical composition comprising citrate and/or phosphate, as required by claims 13 and 14. Furthermore, US 6,060,382 fails to teach or suggest the other specific ingredients required by the claimed formulations of claims 13-25, which Applicants have demonstrated through a working example in the instant Specification results in a pharmaceutical formulation with both **improved shelf life and the ability to dissolve high concentrations of proteins** (see examples 1 and 2 at pages 28-30 of instant Specification). Applicants submit that it would **not** have been obvious to one of ordinary skill in the art, based on the teachings of US 6,060,382 and Gombotz et al., to combine the specific ingredients of the claims to arrive at a pharmaceutical formulation with **improved stability and/or a high protein concentration**.

As indicated above, the claimed formulations are inventive in that they embody Applicants' **unexpected discovery** that the claimed formulations are effective in **improving the stability of an antibody at high antibody concentration in the liquid state**. US 6,060,382 fails to teach or suggest pharmaceutical formulations comprising **a liquid aqueous formulation comprising an antibody with improved stability and/or a high protein concentration**. Thus, US 6,060,382 would not render the claimed invention obvious to the ordinarily skilled artisan.

As evidenced by the foregoing, Gombotz et al. and US 6,060,382 in combination fail to teach or suggest each and every element of claims 1-25 presented and, accordingly, US 6,060,382 fails to render these claims obvious.

Conclusion

In view of the foregoing amendments and remarks, Applicants believe that the rejections set forth in the Office Action dated March 3, 2009 have been overcome and consequently that the application is in condition for allowance. Applicants therefore respectfully request reconsideration and removal of the rejections, and allowance of the claims as amended.

Respectfully submitted,

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